

# Modern Concepts of Cardiovascular Disease

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## BACTERIAL ENDOCARDITIS

Bacterial endocarditis, even after a decade's experience with antibiotics, remains a difficult therapeutic problem. While the incidence of this infection may have fallen slightly as a result of the widespread use of antibiotics, it still is a relatively common complication of rheumatic and congenital heart disease and must be considered every time a febrile illness occurs in patients with these conditions. Furthermore, in spite of the increasing number of antibiotics available, the mortality from bacterial endocarditis has not decreased appreciably in the past five years, being still in the neighborhood of 30 per cent. Since most of the deaths are now attributable to complications, particularly heart failure and major embolic accidents, early recognition and eradication of the infection offer the main approaches to improving therapeutic results. The infectious agent can be eliminated in better than 90 per cent of cases, but, if this is not accomplished before irreversible valvular or myocardial damage has occurred, or before there has been a cerebral embolus, the patient may be dead or incapacitated in spite of a bacteriologic cure. Hence, early diagnosis is extremely important.

### DIAGNOSIS

Usually the onset of subacute bacterial endocarditis is insidious, and its manifestations are so protean that early recognition is difficult. The patient may pass off his symptoms as "flu" for weeks or months without ever consulting a physician. One important step, then, is to educate patients with valvular heart disease as to the importance of consulting their physician whenever they are not feeling well and particularly whenever they have fever for more than a few days. This can and should be done without frightening the patient unnecessarily. He can at the same time be reassured that, if the infection is detected and treated early, a favorable outcome is almost certain.

In the first few weeks of the disease many of the classical features of bacterial endocarditis are frequently absent. The patient may

not feel or look particularly ill. Embolic lesions, splenomegaly, clubbing of the fingers and anemia are helpful diagnostically if present but usually do not occur until the disease is well established. The only features which are almost always present at least in some degree are a *heart murmur* and *fever*. In any event, all patients exhibiting these two findings must be suspected of having bacterial endocarditis, and multiple blood cultures as well as appropriate studies to rule out other causes of fever are in order. If organisms are recovered from several blood cultures, the diagnosis is virtually established. However, in some cases blood cultures remain negative, especially when the patient has already received some antibiotic therapy. While it is highly desirable to identify the infecting organism so that its reaction to various antibiotics can be measured, there are times when one has to treat the patient without the help of an established etiologic diagnosis. Should there be a reasonable possibility on clinical grounds that the patient might have bacterial endocarditis, five or six blood cultures should be taken (at hourly intervals if the need for therapy seems urgent) and then treatment should be started without waiting for the results. Therapy can be modified later if the patient's response or the bacteriologic findings so indicate.

One of the most difficult differential diagnoses is that between rheumatic activity and bacterial endocarditis, not only because they have many clinical features in common, but also because in a small number of cases the two conditions coexist. If a patient over the age of ten who has been suspected of having chronic rheumatic activity runs an atypical course and does poorly on anti-rheumatic measures, it is probably wise to give an intensive course of penicillin and streptomycin even though the diagnosis of bacterial endocarditis cannot be established.

### THERAPY

The treatment of bacterial endocarditis caused by penicillin-sensitive green (viridans) streptococci presents few problems.

Patients with such infections can almost always be cured by an intensive course of penicillin (10 to 15 million units daily) given for two weeks. There is considerable evidence that adding streptomycin (1 to 2 grams daily) to the above regimen increases its effectiveness without great risk of streptomycin toxicity.

In recent years, unfortunately, a smaller proportion of patients with bacterial endocarditis have been found to harbor penicillin-sensitive streptococci, and more patients infected by enterococci and penicillin-resistant staphylococci have been encountered. The latter patients together with those from whom no organisms are recovered and those whose disease is caused by a great variety of unusual organisms present a much more complicated therapeutic problem.

The guiding principle of antibiotic treatment of bacterial endocarditis should be the selection of the agent, or combination of agents, which offers the best hope of complete and rapid sterilization of the vegetations. To do this one cannot rely on antibacterial substances which are primarily bacteriostatic in their action, such as the sulfonamides and the newer broad spectrum antibiotics. Antagonism between these agents and penicillin has been demonstrated in vitro and in animals under certain circumstances, and, therefore, for the present their combination with penicillin in treating bacterial endocarditis should generally be avoided even though the clinical importance of antibiotic antagonism remains to be proven. Ideally, the determination of the optimum treatment in penicillin-resistant infections should be based upon studies of the infecting organism recovered from each patient and these studies should include procedures which measure the bactericidal effects of the antibiotics tested. When such information is not available, one must be guided by probabilities based upon experience with other cases.

Enterococcal endocarditis can usually be cured by high doses of penicillin (10 to 20 million units a day) plus streptomycin (1 to 2 grams a day) administered for six weeks. A longer course seems to be more necessary for enterococcal endocarditis than for the usual streptococcus viridans infection probably because enterococci are killed very slowly even by optimum concentrations of antibiotics. Streptomycin is added to the regimen because it has been shown repeatedly that, while it is ineffective by itself, it greatly enhances the killing effect of penicillin for this organism. Vestibular damage is likely to occur

from the use of this drug, but in such cases the risk seems justifiable. Most enterococci are quite "sensitive" to aureomycin, terramycin and chloramphenicol, but clinical results with these three agents have been disappointing—far inferior to those obtained with penicillin plus streptomycin.

Staphylococci are even more difficult to deal with, not only because they are more invasive and cause more rapid tissue destruction than the non-hemolytic streptococci, but also because in recent years a high proportion of strains encountered in human infections have been resistant to penicillin, and a few have been resistant to all available antibiotics. The variation among strains is tremendous, and no general rules of therapy can be laid down at present except to say that, if the organism is resistant to penicillin, one can try aureomycin or terramycin, or one of these combined with streptomycin or penicillin, for four to six weeks with some hope of cure. The new antibiotic erythromycin is also worth considering in resistant staphylococcal infections, but experience with it is meager.

## PROPHYLAXIS

It is not feasible to administer running doses of antibiotics month in and month out to prevent bacteremias and hence to give complete protection to people with known predisposing heart disease. In fact, we have no sure means of completely preventing bacteremia, even over a short time following tooth extraction. Penicillin does, however, decrease the frequency and intensity of bacteremia, and, if kept up for a sufficient time, at least forty-eight hours, will probably kill any organisms reaching the heart valve before a vegetation is formed. Patients with valvular heart disease should be educated concerning the need for prophylaxis at the time of operative procedures, particularly in the mouth, nasopharynx, bowel or genitourinary tract. One to two million units of penicillin daily given in repository form every twelve hours are probably effective in most instances, but no one regimen has been thoroughly proven.

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The opinions and conclusions expressed herein are those of the author and do not necessarily represent the official views of the Scientific Council of the American Heart Association.

